REMARKS

Claims 1, 2, 4 – 7, 15, 22, 28, 48 and 96 - 98 are pending in the application. Claims 3, 5, 8 - 14, 16 – 21, 23 – 27, 29 – 47, and 49 – 96 have been cancelled. Claims 1 – 7, 15, 22, 28 and 48 are under consideration. Claims 1 and 15 have been amended. No new claims have been added. No new matter has been added by virtue of these amendments; support therefore can be found in throughout the specification and original claims of the application.

Any cancellation of the claims should in no way be construed as acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

Applicant responds to the prior Office Action as follows.

Claim Rejections Withdrawn 35 USC § 102(b)

The Examiner has withdrawn the rejection of claims 1, 2, 7, 15 and 48 under 35 USC § 102 (b) as being anticipated by Vadaie et al. (Glycobiology, 2002 Oct; 12 (10): 589-97).

Claim Rejections 35 USC § 112, second paragraph

The Examiner has rejected claims 1 – 2, 7, 15, 22, 28 and 48 under 35 USC § 112, second paragraph, for being allegedly indefinite. (Office Action, p.2). Applicants respectfully traverse this rejection.

The present claims recite a purified and isolated catalytic domain from a β(1,4)-galactosyltransferase I corresponding to SEQ ID NO: 6, and consisting of a conservative amino acid exchange at amino acid position 344 of SEQ ID NO: 6, wherein the amino acid exchange at position 344 of SEQ ID NO: 6 is selected from M344H, M344E, M344A, M344S, or M344Q, and wherein the catalytic domain catalyzes formation of galactose- ß(1,4)-N- acetylglucosamine bond in the presence of magnesium, and further comprising a conservative amino acid exchange at an amino acid position corresponding to amino acid position 342 of SEQ ID NO: 6.

The Examiner argues that "(c)laims 1 and 15 are indefinite in the recitation 'a purified and isolated catalytic domain from β(1,4)-galactosyltransferase I consisting of SEQ ID NO: 6 and comprising a conservative amino acid exchange at amino acid position 344,' which is confusing because it is not clear as to the phrase 'amino acid exchange at position 344' refers to what protein?" (Office Action, p.3).

Applicants have amended the claims to recite that the conservative amino acid exchange is at amino acid position 344 of SEQ ID NO: 6.

Accordingly, Applicants respectfully request that the rejection be withdrawn.

Claim Rejections 35 USC § 112, first paragraph

The Examiner has rejected claims 1, 2, 4 – 6, 7, 15, 22, 28 and 48 under 35 USC § 112, first paragraph, as allegedly failing to comply with the written description requirement. (Office Action, p.3). Applicants respectfully traverse the rejection.

Present claim 1 is directed to a purified and isolated catalytic domain from a β(1,4)-galactosyltransferase I corresponding to SEQ ID NO: 6, and consisting of a conservative amino acid exchange at amino acid position 344 of SEQ ID NO: 6, wherein the amino acid exchange at position 344 of SEQ ID NO: 6 is selected from M344H, M344E, M344A, M344S, or M344Q, and wherein the catalytic domain catalyzes formation of galactose- ß(1,4)-N- acetylglucosamine bond in the presence of magnesium, and further comprising a conservative amino acid exchange at an amino acid position corresponding to amino acid position 342 of SEQ ID NO: 6.

Present claim 15 is directed to a purified and isolated catalytic domain from a β(1,4)-galactosyltransferase I corresponding to SEQ ID NO: 6, and consisting of a conservative amino acid exchange at amino acid position 344 of SEQ ID NO: 6, wherein the amino acid exchange at position 344 of SEQ ID NO: 6 is selected from M344H, M344E, M344A, M344S, or M344Q, and wherein the catalytic domain catalyzes formation of an N-acetylgalactosamine- β(1,4)-N-acetylglucosamine bond in the presence of magnesium.

The Examiner argues that the claims "are directed to any non-mutated or mutated catalytic domain from any galactosyltransferase I isolated from any source or man made having any structural feature comprising a conservative amino acid exchange at position 344 and 342 (claims 1 and 6) corresponding to SEQ ID NO: 6, which catalyses the formation of galactose- ß(1,4)-N- acetylglucosamine bond in the presence of magnesium." (Office Action, p.3 - 4).

Without acquiescing to the validity of the rejection and solely in the interest of advancing prosecution, Applicants have amended the claims to recite a purified and isolated catalytic domain from a β(1,4)-galactosyltransferase I corresponding to SEQ ID NO: 6, and consisting of a conservative amino acid exchange at amino acid position 344 of SEQ ID NO: 6, wherein the amino acid exchange at position 344 of SEQ ID NO: 6 is selected from M344H, M344E, M344A, M344S, or M344Q.

The specification provides sufficient description of the isolated catalytic domain as claimed. For example at p. 7, lines 25 of the specification, Applicants teach:

> For example, a catalytic domain may be from, but is not limited to bovine β (1,4)-Galactosyltransferase I (Seq ID NO: 6), the catalytic domain from human β (1,4)-Galactosyltransferase I (Seq ID NO: 4), or the catalytic domain from mouse β (1,4)-Galactosyltransferase I (Seq ID NO: 5). A catalytic domain may have an amino acid sequence found in a wild-type enzyme, or may have an amino acid sequence that is different from a wild-type sequence. For example, a catalytic domain may have an amino acid sequence that corresponds to amino acid residues 130-402 of SEQ ID NO: 6, expect that the methionine is exchanged with histidine at amino acid position 344.

Accordingly, Applicants respectfully request that the foregoing rejection be withdrawn.

The Examiner has rejected claims 1, 2, 4 – 6, 7, 15, 22, 28 and 48 under 35 USC § 112, first paragraph. (Office Action, p.6). The Examiner argues that the specification, while being enabling for mutated catalytic domains of a galactosyltransferase I of SEQ ID NO: 6, which catalyses formation of galactose β(1,4)-N-acetylglucosamine bond in the presence of magnesium, wherein the mutations are at positions 344, 342, 228 and 229 of a galactosyltransferase of SEQ ID NO: 6, does not reasonably provide enablement for any non-mutated or mutated catalytic domain from any galactosyltransferase I isolated from any source comprising a conservative amino acid exchange at position 344 and 342." (Office Action, p.6). Applicants respectfully disagree.

The present claims have been set forth above.

Without acquiescing to the validity of the rejection and solely in the interest of advancing prosecution, Applicants have amended the claims to recite a purified and isolated catalytic domain from a β(1,4)-galactosyltransferase I corresponding to SEQ ID NO: 6, and consisting of a conservative amino acid exchange at amino acid position 344 of SEQ ID NO: 6, wherein the amino acid exchange at position 344 of SEQ ID NO: 6 is selected from M344H, M344E, M344A, M344S, or M344Q.

The specification provides ample teaching to enable one skilled in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the present claims. Applicants describe at p. 10, beginning at line 10, catalytic domains that catalyze formation of a bond between a donor and an acceptor to form ß (galactose1,4)-N-acetylglucosamine bonds. Further, at page 11 of the application, for example, Applicants describe one such particular exchange, M344H:

> In the presence of Mg^{2+}, the mutant, M344H-Gal-T1, exhibited 25% of the catalytic activity observed with the wild-type enzyme in the presence of Mn^{+}. It also has higher Km for the substrates. The crystal structures of M344H-Gal-T1 in complex with either UDP-Gal Mn^{+}+ or UDP-Gal Mg^{2+}, and the crystal structure of M344E-Gal-T1 in complex with UDP-Gal Mn^{2+}, have been determined at 2.3 ANG. resolutions. The structures show that the coordination stereochemistry of Mg^{2+} is quite similar to that of Mn^{2+}. Both His344 and Glu344

> in the mutants exhibit stronger coordination bonds with the metal ion compared to Met344 in the wild-type enzyme. This strong metal-ion coordination in the mutants appears to reduce k_{cat} by interfering with the ability of the long flexible loop to undergo the required conformational changes during the catalytic cycle, but also by interfering with the formation of the transition state complex.

Further, Applicants teach the metal specificity of the mutants, where:

> ...it was determined that the mutant M344H-Gal-T1, in the presence of Mn^{2+}, has only 1.5% of the wild-type enzyme activity. On the other hand, the mutant M344H-Gal-T1 exhibits 25% of its catalytic activity in the presence of an alkali metal ion, Mg^{2+}. In contrast, Mg^{2+} does not activate the wild-type enzyme. Although metal ions Mg^{2+} and Mn^{2+} bind to the mutant M344H-Gal-T1, their enzyme kinetics are different, indicating that the residue at position 344 and the appropriate metal ion play an important role in the conformational dynamics of the long loop in the catalytic mechanism of ß4Gal-T1.

Applicants also teach that amino acid residues that are involved with metal binding and that can be mutated can optionally include an additional mutation corresponding to amino acid position 342. For example, at p. 11, Applicants teach that "such a mutation may include exchange of cysteine at amino acid position 342 with threonine (C342T). However, other amino acids may be exchanged for cysteine that provide an active catalytic domain."

Accordingly, the teachings of the specification enable one of skill in the art to practice the full scope of the claimed invention. Applicants request that the rejection be reconsidered and withdrawn.

Claim Rejections 35 USC § 102(b)

The Examiner has rejected claims 7, 28 and 48 under 35 USC § 102 (b) as being allegedly anticipated by Boggeman et al. (Glycobiology 13(11), Nov 2003, p.869, and

8th annual conference of the Society for Glycobiology). (Office Action, p.11). Applicants respectfully traverse the rejection.

Claim 7 depends from claim 1 and recites a polypeptide comprising the catalytic domain according to claim 1.

The present application claims priority from U.S. Provisional Application Ser. No. 60/527,615, filed on December 5, 2003.

The Examiner improperly cites the Boegmann et al. publications (Glycobiology November 2003 and Annual Conference for the Society for Glycobiology December 2003) as 102(b) references. Neither of the Boegmann publications are available as 102(b) references against the present invention.

Further, in order to anticipate a claim, each and every element of the claim must be found in the cited document. This is discussed in the Manual of Patent Examining Procedure, § 2131.

Nowhere do the Boggeman et al. references teach a polypeptide comprising a purified and isolated catalytic domain from a β(1,4)-galactosyltransferase I corresponding to SEQ ID NO: 6, and consisting of a conservative amino acid exchange at amino acid position 344 of SEQ ID NO: 6, wherein the amino acid exchange at position 344 of SEQ ID NO: 6 is selected from M344H, M344E, M344A, M344S, or M344Q, and wherein the catalytic domain catalyzes formation of galactose- ß(1,4)-N-acetylglucosamine bond in the presence of magnesium, and further comprising a conservative amino acid exchange at an amino acid position corresponding to amino acid position 342 of SEQ ID NO: 6.

Applicants respectfully request that the foregoing rejection be withdrawn.

Claim Rejections 35 USC § 103(a)

The Examiner has rejected claims 1 – 2, 4 – 6, 15, 22, 96 – 97 and 98 under 35 USC § 103 (a) as being unpatentable over Boegmann et al. (above) as applied to claims 7, 28 and 48 above, and further in view of Ramakrishnan et al. (J Biol Chem. 2001 Oct 5; 276(40):37665 0 71).

The present claims have been set forth above.

As discussed above, the Boegmann reference is improper. Moreover, the Boegmann reference does not teach the present invention as claimed.

The Ramakrishnan reference does not cure the defects of the Boegmann reference. Nowhere does Ramakrishnan teach a polypeptide comprising a purified and isolated catalytic domain from a β(1,4)-galactosyltransferase I corresponding to SEQ ID NO: 6, and consisting of a conservative amino acid exchange at amino acid position 344 of SEQ ID NO: 6, as claimed, **and wherein the catalytic domain catalyzes formation of galactose- ß(1,4)-N- acetylglucosamine bond in the presence of magnesium**, and further comprising a conservative amino acid exchange at an amino acid position corresponding to amino acid position 342 of SEQ ID NO: 6.

The Examiner argues that "Ramakrishnan et al. teach isolating a mutant catalytic domain of β(1,4)-galactosyltransferase from bovine, wherein the mutation at position 342 is Cys342Thr...(and) Ramakrishnan et al. also teach that lactalbumin stimulates β(1,4)-galactosyltransferase-1 and mutants Cys342Thr catalytic domain activity threefold." (Office Action, p. 13 -14).

Applicants point out a fundamental difference between the experiments carried out in the Ramakrishnan reference and the present claims, that the Ramakrishnan reference examines the complex of Gal-T1 **in the presence of UDP-Glc-Mn**. Only under these conditions**, which are different from the present claims that require magnesium,** Ramakrishnan found that the mutation of Cys-342 to Thr in Gal-T1 enhances the in vitro folding of the protein.

Applicants again point out that in the present invention, "(i)n the presence of Mg2+, the mutant, M344H-Gal-T1, exhibited 25% of the catalytic activity observed with the wild-type enzyme in the presence of Mn+. (p.11, line 1 - 3). Further, referring to Figure 5, for example, Figure 5 shows an acceptor (GlcNAc) activation curve for the M344H-Gal-T1 mutant in the presence of either Mn2+ (closed circles) or Mg^{2+} (open inverted triangles) metal ion. As shown in Figure 5, below, the catalytic activity for the M344H-Gal-T1 mutant is better with the Mg^{2+} than with the Mn^{2+}, preferred by the native enzyme.

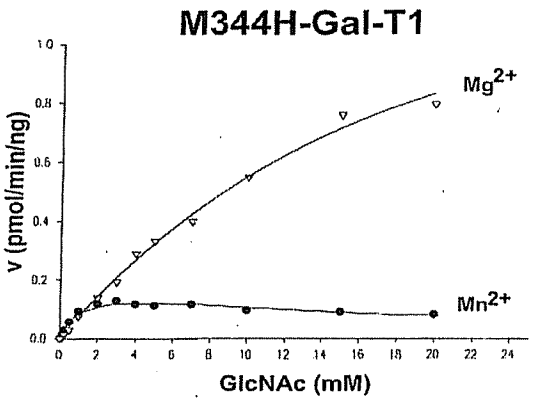

FIG. 5

Accordingly, none of the Boegmann or Ramakrishnan references, alone or together, teach or suggest the present invention, as claimed.

Applicants respectfully request that the foregoing rejection be withdrawn.

CONCLUSION

Early consideration and allowance of the application are earnestly solicited.

Respectfully submitted,

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